

SUMMARY

[0006a] In a first aspect of the present disclosure, there is provided a use of a pharmaceutical composition comprising an antibody that binds human IL-13, in the manufacture of a medicament for treating moderate to severe atopic dermatitis or reducing pruritus associated with atopic dermatitis in a patient who had inadequate response or intolerance to cyclosporine, or cyclosporine is medically inadvisable for the patient, and

wherein the antibody comprises a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH comprises a HCDR1 comprising SEQ ID NO: 1, a HCDR2 comprising SEQ ID NO: 2, and a HCDR3 comprising SEQ ID NO: 3, and the VL comprises a LCDR1 comprising SEQ ID NO: 4, a LCDR2 comprising SEQ ID NO: 5, and a LCDR3 comprising SEQ ID NO: 6.

[0007] Provided herein are methods, uses and pharmaceutical compositions of anti-IL-13 antibodies, such as lebrikizumab, for treating atopic dermatitis or reducing pruritus associated with atopic dermatitis. Also provided herein are doses and dosing regimens for the methods and uses of anti-IL-13 antibodies, such as lebrikizumab, for treating atopic dermatitis or reducing pruritus associated with atopic dermatitis. In some examples, provided herein are methods and uses of anti-IL-13 antibodies for treating atopic dermatitis or reducing pruritus associated with atopic dermatitis in patients with moderate to severe atopic dermatitis that are not adequately controlled with cyclosporine (e.g., inadequate response or intolerance to cyclosporine) or for whom cyclosporine is not medically advisable.

[0008] In one example, provided herein are methods of treating moderate to severe atopic dermatitis or reducing pruritus associated with atopic dermatitis in a patient in need thereof who had inadequate response or intolerance to cyclosporine, or cyclosporine is medically inadvisable for the patient, which comprise administering to the patient a pharmaceutical composition comprising an anti-IL-13 antibody. In some examples, provided herein are methods for treating moderate to severe atopic dermatitis or reducing pruritus, which comprise selecting a patient who has moderate to severe atopic dermatitis and had inadequate response or intolerance to cyclosporine, or cyclosporine is medically inadvisable for the patient, and administering to the patient a pharmaceutical composition comprising an antibody that binds human IL-13. In some examples, the patient is aged 12 years and older. In some examples, the patient has moderate to severe atopic dermatitis for at least a year. In some examples, the patient has an Eczema Area and Severity Index (EASI) score of

16 or greater, an Investigator Global Assessment (IGA) score of 3 or greater, and more than 10% of body surface area (BSA) affected by atopic dermatitis, before administration of the pharmaceutical composition.

[0009] Also provided herein are methods for treating moderate to severe atopic dermatitis or reducing pruritus associated with atopic dermatitis, which comprise selecting a patient who (i) is aged 12 years and older; (ii) has chronic atopic dermatitis according to Hanifin and Rajka Criteria for more than a year; (iii) has an EASI score of 16 or greater; (iv) has an IGA score of 3 or greater; (v) has more than 10% of BSA affected by atopic dermatitis; (vi) had inadequate response to topical corticosteroids; and (vii) had inadequate response or intolerance to cyclosporine, or cyclosporine is medically inadvisable for the patient, and administering to the patient a pharmaceutical composition comprising an antibody that binds human IL-13.

[0010] In some examples, the cyclosporine is cyclosporine A (CsA). In some examples, the patient had inadequate response to cyclosporine (e.g., CsA), e.g., at least 4

weeks prior to administering the pharmaceutical composition. In some examples, the patient had intolerance to cyclosporine (e.g., CsA). In some examples, cyclosporine is medically inadvisable for the patient due to one of the following reasons: (i) medical contraindications, (ii) use of prohibited concomitant medications, (iii) increased susceptibility to cyclosporine -induced renal damage and/or liver damage, (iv) increased risk of serious infections, or (v) hypersensitivity to cyclosporine active substance or excipients. In some examples, the patient had inadequate response to topical corticosteroids.

[0011] In some examples, the anti-IL-13 antibody binds IL-13 with high affinity and blocks signaling through the active IL-4Ralpha/IL-13Ralpha1 heterodimer. In some examples, the anti-IL-13 antibody comprises a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH comprises a HCDR1 comprising SEQ ID NO: 1, a HCDR2 comprising SEQ ID NO: 2, and a HCDR3 comprising SEQ ID NO: 3, and the VL comprises a LCDR1 comprising SEQ ID NO: 4, a LCDR2 comprising SEQ ID NO: 5, and a LCDR3 comprising SEQ ID NO: 6. In some examples, the anti-IL-13 antibody comprises a VH comprising SEQ ID NO: 7, and a VL comprising SEQ ID NO: 8. In some examples, the anti-IL-13 antibody comprises a heavy chain comprising SEQ ID NO: 9, and a light chain comprising SEQ ID NO: 10. In some examples, the anti-IL-13 antibody is lebrikizumab.

[0012] In some examples, the pharmaceutical composition comprises 250 mg or 500 mg of the anti-IL-13 antibody. In some examples, the pharmaceutical composition is administered subcutaneously to the patient.

[0013] In some examples, the patient is treated with the pharmaceutical composition for a period of about 16 - 52 weeks. In some examples, the patient is treated with the pharmaceutical composition for a treatment period (or an induction period), e.g., about 16 weeks. During this treatment period of 16 weeks, the patient is treated with a loading dose of the pharmaceutical composition comprising 500 mg of the antibody once every two weeks for two doses, and a subsequent dose of the pharmaceutical composition comprising 250 mg of the antibody once every two weeks for seven doses.

[0014] After completion of the treatment period or induction period, the patient enters a maintenance period, e.g., up to 36 weeks. In some examples, the patient is treated with a maintenance dose of the pharmaceutical composition comprising 250 mg of the antibody once every two weeks during the maintenance period.

[0015] In another example, provided herein are pharmaceutical composition comprising an anti-IL-13 antibody for use in the treatment of moderate to severe atopic dermatitis or reducing pruritus in a patient who had inadequate response or intolerance to cyclosporine, or cyclosporine is

medically inadvisable for the patient. Also provided herein are pharmaceutical composition comprising an anti-IL-13 antibody for use in the treatment of moderate to severe atopic dermatitis or reducing pruritus in a patient who (i) is aged 12 years and older; (ii) has chronic atopic dermatitis according to Hanifin and Rajka Criteria for more than a year; (iii) has an EASI score of 16 or greater; (iv) has an IGA score of 3 or greater; (v) has more than 10% of BSA affected by atopic dermatitis; (vi) had inadequate response to topical corticosteroids; and (vii) had inadequate response or intolerance to cyclosporine, or cyclosporine is medically inadvisable for the patient. In some examples, the pharmaceutical composition is for subcutaneous administration to the patient.

[0016] In another example, provided herein are uses of a pharmaceutical composition comprising an anti-IL-13 antibody in the manufacture of a medicament for the treatment of moderate to severe atopic dermatitis or reducing pruritus in a patient who had inadequate response or intolerance to cyclosporine, or cyclosporine is medically inadvisable for the patient. Also provided herein are uses of a pharmaceutical composition comprising an anti-IL-13 antibody in the manufacture of a medicament for the treatment of moderate to severe atopic dermatitis or reducing pruritus in a patient who (i) is aged 12 years and older; (ii) has chronic atopic dermatitis according to Hanifin and Rajka Criteria for more than a year; (iii) has an EASI score of 16 or greater; (iv) has an IGA score of 3 or greater; (v) has more than 10% of BSA affected by atopic dermatitis; (vi) had inadequate response to topical corticosteroids; and (vii) had inadequate response or intolerance to cyclosporine, or cyclosporine is medically inadvisable for the patient. In some examples, the pharmaceutical composition is for subcutaneous administration to the patient.

[0017] In some examples, the methods, uses, and pharmaceutical compositions described herein further comprise administering one or more topical corticosteroids to the patient. In some examples, the topical corticosteroid is triamcinolone acetonide, hydrocortisone, or a combination of triamcinolone acetonide and hydrocortisone. In some examples, the topical corticosteroids are administered concomitantly with the anti-IL-13 antibody.

BRIEF DESCRIPTION OF THE DRAWINGS

[0018] Figure 1 is a schematic diagram of the Phase 3 study design described in Example 1.

DETAILED DESCRIPTION

[0019] Provided herein are methods, uses and pharmaceutical compositions of anti-IL-13 antibodies for treating atopic dermatitis or reducing pruritus associated with atopic dermatitis. Also

CLAIMS

1. Use of a pharmaceutical composition comprising an antibody that binds human IL-13, in the manufacture of a medicament for treating moderate to severe atopic dermatitis or reducing pruritus associated with atopic dermatitis in a patient who had inadequate response or intolerance to cyclosporine, or cyclosporine is medically inadvisable for the patient, and wherein the antibody comprises a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH comprises a HCDR1 comprising SEQ ID NO: 1, a HCDR2 comprising SEQ ID NO: 2, and a HCDR3 comprising SEQ ID NO: 3, and the VL comprises a LCDR1 comprising SEQ ID NO: 4, a LCDR2 comprising SEQ ID NO: 5, and a LCDR3 comprising SEQ ID NO: 6.
2. The use of claim 1, wherein the patient:
 - i. is aged 12 years and older;
 - ii. has chronic atopic dermatitis according to Hanifin and Rajka Criteria for more than a year;
 - iii. has an Eczema Area and Severity Index (EASI) score of 16 or greater;
 - iv. has an Investigator Global Assessment (IGA) score of 3 or greater;
 - v. has more than 10% of body surface area (BSA) affected by atopic dermatitis; and/or
 - vi. had inadequate response to topical corticosteroids.
3. The use of claim 1 or 2, wherein the cyclosporine is cyclosporine A.
4. The use of any one of claims 1-3, wherein the patient had inadequate response to cyclosporine.
5. The use of claim 4, wherein the pharmaceutical composition is to be administered to the patient, and wherein the patient had inadequate response to cyclosporine at least 4 weeks prior to administration of the pharmaceutical composition.
6. The use of any one of claims 1-3, wherein the patient had intolerance to cyclosporine.

7. The use of any one of claims 1-3, wherein cyclosporine is medically inadvisable for the patient due to one of the following reasons:
 - i. medical contraindications,
 - ii. use of prohibited concomitant medications,
 - iii. increased susceptibility to cyclosporine-induced renal damage and/or liver damage,
 - iv. increased risk of serious infections, or
 - v. hypersensitivity to cyclosporine active substance or excipients.
8. The use of any one of claims 1-7, wherein the pharmaceutical composition is to be administered to the patient, and wherein the patient had inadequate response to topical corticosteroids at least two weeks prior to administration of the pharmaceutical composition.
9. The use of any one of claims 1-8, wherein the patient has no prior exposure to dupilumab.
10. The use of any one of claims 1-8, wherein the patient has prior exposure to dupilumab.
11. The use of any one of claims 1-10, wherein the antibody comprises a VH comprising SEQ ID NO: 7, and a VL comprising SEQ ID NO: 8.
12. The use of any one of claims 1-11, wherein the antibody comprises a heavy chain comprising SEQ ID NO: 9, and a light chain comprising SEQ ID NO: 10.
13. The use of any one of claims 1-12, wherein the antibody is lebrikizumab.
14. The use of any one of claims 1-13, wherein the pharmaceutical composition comprises 250 mg or 500 mg of the antibody.
15. The use of any one of claims 1-14, wherein the pharmaceutical composition is to be administered subcutaneously to the patient.
16. The use of any one of claims 1-15, wherein the pharmaceutical composition is to be administered subcutaneously to the patient once every two weeks.

17. The use of any one of claims 1-16, wherein the patient is to be treated with the pharmaceutical composition for a period of 16 - 52 weeks.
18. The use of any one of claims 1-17, wherein the patient is to be treated with the pharmaceutical composition for a treatment period of 16 weeks.
19. The use of claim 18, wherein, during the treatment period, the patient is to be treated with a loading dose of the pharmaceutical composition comprising 500 mg of the antibody once every two weeks for two doses, and a subsequent dose of the pharmaceutical composition comprising 250 mg of the antibody once every two weeks for seven doses.
20. The use of any one of claims 1-19, wherein the pharmaceutical composition is to be administered to the patient, and wherein the patient is to be further treated with the pharmaceutical composition for a maintenance period up to 36 weeks.
21. The use of claim 20, wherein the patient is to be treated with a maintenance dose of the pharmaceutical composition comprising 250 mg of the antibody once every two weeks during the maintenance period.
22. The use of claim 20, wherein the patient is to be treated with a maintenance dose of the pharmaceutical composition comprising 250 mg of the antibody once every four weeks during the maintenance period.
23. The use of any one of claims 1-22, wherein one or more of the following characteristics of the patient are determined after the treatment period and/or the maintenance period:
 - i. EASI score;
 - ii. IGA score;
 - iii. Percentage of BSA affected by atopic dermatitis;
 - iv. Pruritus numeric rating scale (NRS) score;
 - v. Severity Scoring of Atopic Dermatitis (SCORAD);
 - vi. Sleep loss scale;
 - vii. Skin pain NRS score;
 - viii. Patient-Oriented Eczema Measure (POEM) total score;

- ix. Dermatology Life Quality Index (DLQI) score, Children Dermatology Life Quality Index (CDLQI), or DLQI-Relevant (DLQI-R) score;
- x. World Health Organisation - Five Well-Being Index (WHO-5) score;
- xi. Recap of Atopic Eczema (RECAP) score;
- xii. Treatment Satisfaction Questionnaire for Medication - 9 items (TSQM-9) score.

24. The use of any one of claims 1-23, wherein the pharmaceutical composition is to be administered to the patient using a subcutaneous administration device.

25. The use of claim 24, wherein the subcutaneous administration device is selected from a prefilled syringe, disposable pen injection device, microneedle device, microinfuser device, needle-free injection device, or autoinjector device.

26. The use of any one of claims 1-25, wherein the pharmaceutical composition is to be administered to the patient in combination with one or more topical corticosteroids.

27. The use of claim 26, wherein the one or more topical corticosteroids is triamcinolone acetonide, hydrocortisone, or a combination of triamcinolone acetonide and hydrocortisone.

28. The use of claim 26 or 27, wherein the one or more topical corticosteroids is to be administered concomitantly to the patient with the antibody.